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APPLICATION NO.	FILING DATE	FIRST NAMED INVENTOR	ATTORNEY DOCKET NO.	CONFIRMATION NO.
10/691,330	10/22/2003	Istvan Boldogh	265.00390101	1384

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EXAMINER	
KAM, CHIH MIN	

ART UNIT	PAPER NUMBER
1656	

MAIL DATE	DELIVERY MODE
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Please find below and/or attached an Office communication concerning this application or proceeding.

The time period for reply, if any, is set in the attached communication.

Office Action Summary	Application No.	Applicant(s)	
	10/691,330	BOLDOGH ET AL.	
	Examiner	Art Unit	
	Chih-Min Kam	1656	

-- The MAILING DATE of this communication appears on the cover sheet with the correspondence address --

Period for Reply

A SHORTENED STATUTORY PERIOD FOR REPLY IS SET TO EXPIRE 3 MONTH(S) OR THIRTY (30) DAYS, WHICHEVER IS LONGER, FROM THE MAILING DATE OF THIS COMMUNICATION.

- Extensions of time may be available under the provisions of 37 CFR 1.136(a). In no event, however, may a reply be timely filed after SIX (6) MONTHS from the mailing date of this communication.
- If NO period for reply is specified above, the maximum statutory period will apply and will expire SIX (6) MONTHS from the mailing date of this communication.
- Failure to reply within the set or extended period for reply will, by statute, cause the application to become ABANDONED (35 U.S.C. § 133). Any reply received by the Office later than three months after the mailing date of this communication, even if timely filed, may reduce any earned patent term adjustment. See 37 CFR 1.704(b).

Status

1)☒ Responsive to communication(s) filed on *25 April 2007*.

2a)☐ This action is **FINAL**. 2b)☒ This action is non-final.

3)☐ Since this application is in condition for allowance except for formal matters, prosecution as to the merits is closed in accordance with the practice under *Ex parte Quayle*, 1935 C.D. 11, 453 O.G. 213.

Disposition of Claims

4)☒ Claim(s) *1-6,8,12-15 and 25-32* is/are pending in the application.

4a) Of the above claim(s) *29 and 30* is/are withdrawn from consideration.

5)☐ Claim(s) _____ is/are allowed.

6)☒ Claim(s) *1-6,8,12-15,25-28,31 and 32* is/are rejected.

7)☐ Claim(s) _____ is/are objected to.

8)☐ Claim(s) _____ are subject to restriction and/or election requirement.

Application Papers

9)☐ The specification is objected to by the Examiner.

10)☒ The drawing(s) filed on *22 October 2003* is/are: a)☒ accepted or b)☐ objected to by the Examiner.

Applicant may not request that any objection to the drawing(s) be held in abeyance. See 37 CFR 1.85(a).

Replacement drawing sheet(s) including the correction is required if the drawing(s) is objected to. See 37 CFR 1.121(d).

11)☐ The oath or declaration is objected to by the Examiner. Note the attached Office Action or form PTO-152.

Priority under 35 U.S.C. § 119

12)☐ Acknowledgment is made of a claim for foreign priority under 35 U.S.C. § 119(a)-(d) or (f).

a)☐ All b)☐ Some * c)☐ None of:

1.☐ Certified copies of the priority documents have been received.

2.☐ Certified copies of the priority documents have been received in Application No. _____.

3.☐ Copies of the certified copies of the priority documents have been received in this National Stage application from the International Bureau (PCT Rule 17.2(a)).

* See the attached detailed Office action for a list of the certified copies not received.

Attachment(s)

1) ☐ Notice of References Cited (PTO-892)
2) ☐ Notice of Draftsperson's Patent Drawing Review (PTO-948)
3) ☒ Information Disclosure Statement(s) (PTO/SB/08) Paper No(s)/Mail Date *4/25/07*.
4) ☐ Interview Summary (PTO-413) Paper No(s)/Mail Date. _____ .
5) ☐ Notice of Informal Patent Application
6) ☐ Other: _____.

DETAILED ACTION

1. The Request for Continued Examination (RCE) filed on April 25, 2007 under 37 CFR 1.114 is acknowledged. An action on the RCE follows.

Status of the Claims

2. Claims 1-6, 8, 12-15 and 25-32 are pending.

Applicants' amendment filed April 25, 2007 is acknowledged. Applicants' response has been fully considered. New claims 25-32 have been added. Newly submitted claims 25-32, containing SEQ ID NO:9-34, are directed to an invention that is independent or distinct from the invention originally claimed for the following reasons: The amino acid sequences of SEQ ID NO:9-34, which contain different amino acid sequences and have different effects from the amino acid sequences of SEQ ID NO:1-8, are patentably distinct from the elected amino acid sequences of SEQ ID NO:1-8. Furthermore, if SEQ ID NO:9-34 were included for examination, it would require additional sequence searches for SEQ ID NO:9-34, which would place serious search burden on the Examiner.

Since applicant has received an action on the merits for the originally presented invention, this invention has been constructively elected by original presentation for prosecution on the merits. Accordingly, claims 29-30 (directed to SEQ ID NO:9-33) and claims 25-28, 31-32 (in part; directed to SEQ ID NO:9-34), are withdrawn from consideration as being directed to a non-elected invention. See 37 CFR 1.142(b) and MPEP § 821.03. Therefore, claims 1-6, 8, 12-15 and claims 25-28, 31-32 (in part), directed to a constituent peptide of colostrinin selected from the group consisting of SEQ ID NO:1-8 and/or colostrinin, are examined.

Restriction Requirement

3. Applicants traverse the restriction requirement mailed February 8, 2005. Applicants indicate that the rejection of claims 1-6, 8, and 12-15 under the judicially created doctrine of obviousness-type double patenting as being unpatentable over claims 1-8 of U.S. Patent No. 6,500,798 is improper. However, if the Examiner continues to maintain this obviousness-type double patenting rejection, Applicants submit that all thirty-four sequences of SEQ ID NO:1-34 must properly be examined in the present application. Claims 1-8 of U.S. Patent No. 6,500,798 are drawn to SEQ ID NO:1 through SEQ ID NO:34. Thus, SEQ ID NO:1 through SEQ ID NO:34 have been previously searched and examined by the U.S. Patent and Trademark Office. If the Examiner continues to maintain that the methods of the present invention and the methods of U.S. Patent No. 6,500,798 are not patentably distinct, and as each of SEQ ID NO: 1-34 have already been searched and examined by the U.S. Patent and Trademark Office, Applicants submit that methods drawn to SEQ ID NO: 1 through SEQ ID NO:34 can be readily examined in the present application without placing undue burden on the Examiner. Thus, Applicants submit that new claims 25 and 26 properly belong with the present invention. If the rejection of claims 1-6, 8, and 12-15 under the judicially created doctrine of obviousness-type double patenting as being unpatentable over claims 1-10 of U.S. Patent No. 6,903,068 is maintained, new claims 29 and 30 properly belong with the present invention. If the rejection of claims 1-6, 8, and 12-15 under the judicially created doctrine of obviousness-type double patenting as being unpatentable over claims 1-7 of U.S. Patent No. 7,119,064 is maintained, new claims 31 and 32 properly belong with the present invention. If the rejection of claims 1-6, 8, and 12-15 under the judicially created doctrine of obviousness-type double patenting as being unpatentable over U.S.

Patent Nos. 6,500,798, 6,903,068 and 7,119,064 is maintained, new claims 27 and 28 properly belong with the present invention. Therefore, the examination of new claims 25-32 along with 1-6, 8 and 12-15 is requested (pages 7-8 of the response).

Applicants' response has been fully considered. Regarding including the amino acid sequences of SEQ ID NOs: 9-34 for examination in the present application, the arguments are not found persuasive because of the following reasons. As indicated in paragraph 2 above, since applicant has received an action on the merits for the originally presented invention (SEQ ID NOs:1-8), this invention has been constructively elected by original presentation for prosecution on the merits. Furthermore, to examine SEQ ID NO:9-34 would require additional sequence searches for SEQ ID NO:9-34 for the present application, which would place serious search burden on the Examiner. The sequence search of SEQ ID NO:9-34 is required if these sequences are going to be examined in the instant application, it does not depend on whether these sequences have been search previously (e.g., in U.S. Patent 6,500,798) or not. Moreover, claims 1-10 of U.S. Patent No. 6,903,068 are directed to SEQ ID NO:1-8 and 34, and claims 1-7 of U.S. Patent No. 7,119,604 are directed to SEQ ID NO:1-8, the claims of these two patent do not encompass SEQ ID NO: 9-33 or 9-34. The rejection of claims 1-6, 8, and 12-15 of instant application is made under the judicially created doctrine of obviousness-type double patenting as being unpatentable over claims 1-8 of U.S. Patent No. 6,500,798, claims 1-10 of U.S. Patent No. 6,903,068, or claims 1-7 of U.S. Patent No. 7,119,604, because the scope of claims of instant application is overlapped with the scope of the claims in the patents, it does not mean the full scope of the claims of the patent (e.g., U. S. Patent 6,500,798) has to be examined in the instant

application. Each patent application is examined according to its own merits. Therefore, SEQ ID NO:9-34 will not be examined in the instant application.

Claim Objections

4. Claims 25-28 and 31-32 are objected to because the claims contain recitation of non-elected amino acid sequences such as SEQ ID NO:9-34.

Claim Rejections - 35 USC § 112

The following is a quotation of the second paragraph of 35 U.S.C. 112:

> The specification shall conclude with one or more claims particularly pointing out and distinctly claiming the subject matter which the applicant regards as his invention.

5. Claims 27-28 are rejected under 35 U.S.C. 112, second paragraph, as being indefinite for failing to particularly point out and distinctly claim the subject matter which applicant regards as the invention.

Claims 27-28 are indefinite because the claim lacks an essential step in the method of inhibiting apoptosis or protecting against DNA damage in a cell. The missing step is the outcome of the treatment, it is not clear what result an effective amount of colostrinin would produce?

Maintained Claim Rejections-Obviousness Type Double Patenting

The nonstatutory double patenting rejection is based on a judicially created doctrine grounded in public policy (a policy reflected in the statute) so as to prevent the unjustified or improper timewise extension of the "right to exclude" granted by a patent and to prevent possible harassment by multiple assignees. See *In re Goodman*, 11 F.3d 1046, 29 USPQ2d 2010 (Fed. Cir. 1993); *In re Longi*, 759 F.2d 887, 225 USPQ 645 (Fed. Cir. 1985); *In re Van Ornum*, 686 F.2d 937, 214 USPQ 761 (CCPA 1982); *In re Vogel*, 422 F.2d 438, 164 USPQ 619 (CCPA 1970);and, *In re Thorington,* 418 F.2d 528, 163 USPQ 644 (CCPA 1969).

A timely filed terminal disclaimer in compliance with 37 CFR 1.321(c) may be used to overcome an actual or provisional rejection based on a nonstatutory double patenting ground provided the conflicting application or patent is shown to be commonly owned with this application. See 37 CFR 1.130(b).

Effective January 1, 1994, a registered attorney or agent of record may sign a terminal disclaimer. A terminal disclaimer signed by the assignee must fully comply with 37 CFR 3.73(b).

6. Previous rejection of claims 1-6, 8 and 12-15 under the judicially created doctrine of obviousness-type double patenting as being unpatentable over claims 1-8 of U. S. Patent 6,500,798 is maintained, and new claims 25-26 are added to the rejection. Although the conflicting claims are not identical, they are not patentably distinct from each other because claims 1-6, 8, 12-15 and 25-26 in the instant application disclose a method for inhibiting apoptosis or a method for protecting against DNA damage in a cell, the method comprising contacting the cell with an apoptosis inhibitor selected from the group consisting of colostrinin, a constituent peptide of colostrinin (SEQ ID NO:1-8) and combination thereof, and the specification indicates UV-irradiation is a major cause of oxidative stress in the cells and may induce apoptosis (Example 8; pages 28-29). This is obvious variation in view of claims 1-8 of the patent which disclose a method for modulating the oxidative stress level in a cell, the method comprising contacting the cell with an oxidative stress regulator under conditions effective to decrease the level of an oxidizing species in the cell in response to an oxidative stress, wherein the oxidative stress regulator is colostrinin, a constituent peptide of colostrinin (SEQ ID NO:1-34), an active analog of a constituent peptide of colostrinin (SEQ ID NO:1-34) and combination thereof. Both sets of claims are directed to a method for inhibiting apoptosis or a method for modulating the oxidative stress level in a cell by contacting the cell with an effective amount of colostrinin, a constituent peptide of colostrinin (e.g., SEQ ID NO:1-8) and combination thereof in response to apoptosis or an oxidative stress such as UV-irradiation, which is the same method step as encompassed by the two methods. Therefore, claims 1-6, 8, 12-15 and 25-26 in instant

application and claims 1-8 of the patent are obvious variations of a method for inhibiting apoptosis or a method for modulating the oxidative stress level in a cell by contacting the cell with an effective amount of colostrinin, a constituent peptide of colostrinin (e.g., SEQ ID NO:1-8) or combination thereof in response to apoptosis or an oxidative stress.

Response to Arguments

Applicants indicate that claims 1-6, 8, and 12-15 of the instant application and claims 1-8 of the U.S. Patent 6,500,798 ('798 patent) are drawn to methods that are patentably distinct from each other because the methods steps and outcomes of claims 1-6, 8, and 12-15 of the instant application when compared to claims 1-8 of the '798 patent are wholly different. The instant specification discloses that the induction of oxidative stress and the induction of apoptosis are mechanistically separate pathways within the cell, thus the method for modulating the oxidative stress in a cell and the method of inhibiting apoptosis or protecting against DNA damage in a cell are not obvious one over the other. Neither the present claims nor the methods of modulating the oxidative stress in a cell are drawn to effecting the overall effect of UVB-radiation. Further, the '798 patent does not support a rejection of the present claims under 35 U.S.C. 102(e) or 103. Thus, claims 1-6, 8, and 12-15 cannot be rejected under the judicially created doctrine of obviousness-type double patenting as being unpatentable over claims 1-8 of the '798 patent (pages 11-14 of the response).

Applicants' response has been considered, however, the arguments are not found persuasive because of the following reasons. The method for inhibiting apoptosis or protecting against DNA damage in a cell of the instant application has the same method step (i.e., contacting the cell with an effective amount of colostrinin, a constituent peptide of colostrinin

and combination thereof in response to apoptosis or an oxidative stress) as the method for modulating the oxidative stress level in a cell of the '798 patent, therefore, it would be expected that the treatment of cell with colostrinin, a constituent peptide of colostrinin (e.g., SEQ ID NO:1-8) or combination thereof produces the desired results (i.e., inhibiting apoptosis or protecting against DNA damage in a cell, or modulating the oxidative stress level in a cell). While induction of oxidative stress by UVB-irradiation and the induction of apoptosis by UVB-irradiation are mechanistically separate pathways within the cell, the UVB-irradiation is one of the condition causing oxidative stress and apoptosis (see Example 8 of the instant application). Since the two methods have the same method steps and would produce the desired results, thus, the method of instant application is obvious variant of the method of the '798 patent. Although the '798 patent is not used for a rejection of the present claims under 35 U.S.C. 102(e) or 103, it does not mean the present claims are not obvious variant of the claims of the '798 patent.

7. Previous rejection of claims 1-6, 8 and 12-15 under the judicially created doctrine of obviousness-type double patenting as being unpatentable over claims 1-10 of U. S. Patent 6,903,068 is maintained, and new claims 25-26 are added to the rejection. Although the conflicting claims are not identical, they are not patentably distinct from each other because claims 1-6, 8, 12-15 and 25-26 in the instant application disclose a method for inhibiting apoptosis or a method for protecting against DNA damage in a cell, the method comprising contacting the cell with an apoptosis inhibitor selected from the group consisting of colostrinin, a constituent peptide of colostrinin (SEQ ID NO:1-8) and combination thereof, and the specification indicates colostrinin induces a variety of cytokines in leukocytes or modulates cytokine production (page 8, lines 11-15; page 22, lines 32-33; page 29, lines 24-30). This is

obvious in view of claims 1-10 of the patent which disclose a method for inducing a cytokine or a method for modulating an immune response in a cell, the method comprising contacting the cell with an immunological regulator under conditions effective to induce a cytokine, wherein the immunological regulator is colostrinin, a constituent peptide of colostrinin (SEQ ID NO:1-8 and 34), an active analog of a constituent peptide of colostrinin (SEQ ID NO:1-8 and 34) and combination thereof. Both sets of claims are directed to a method for inhibiting apoptosis or a method for inducing a cytokine in a cell by contacting the cell with an effective amount of colostrinin, a constituent peptide of colostrinin and combination thereof, which is the same method step as encompassed by the two methods. Therefore, claims 1-6, 8, 12-15 and 25-26 in instant application and claims 1-10 of the patent are obvious variations of a method for inhibiting apoptosis or a method for inducing a cytokine in a cell by contacting the cell with an effective amount of colostrinin, a constituent peptide of colostrinin and combination thereof.

Response to Arguments

Applicants indicate that the present methods of claims 1-6, 8, and 12-15 are patentably distinct from the methods of claims 1-10 of U.S. Patent No. 6,903,068 ('068 patent). The Examiner repeatedly relies on teachings that "colostrinin induces a variety of cytokines in leukocytes or modulates cytokine production" (see pages 4-5, Office Action mailed October 25, 2006, and page 2, Advisory Action mailed January 18, 2007) to substantiate a conclusion that claims 1-6 and 8 of the instant application are obvious variants of claims 1-10 of the '068 patent. Applicants respectfully submit that no teachings in the '068 patent, the instant application, nor in any references provided by the Examiner substantiate the assertion that methods for inducing a cytokine in a cell (the '068 patent) make obvious methods for inhibiting apoptosis and for

protecting against DNA damage in a cell (the instant application). Further, the '068 patent does not support a rejection of the present claims under 35 U.S.C. 102(e) or 103. Thus, claims 1-6, 8, and 12-15 cannot be rejected under the judicially created doctrine of obviousness-type double patenting as being unpatentable over claims 1-10 of the '068 patent (pages 8-10 of the response).

Applicants' response has been considered, however, the arguments are not found persuasive because of the following reasons. The specification of instant application teaches colostrinin induces a variety of cytokines in leukocytes or modulates cytokine production (page 8, lines 11-15; page 22, lines 32-33; page 29, lines 24-30), thus colostrinin can induce a cytokine in a cell. Furthermore, the method for inhibiting apoptosis or protecting against DNA damage in a cell has the same method step (i.e., contacting the cell with an effective amount of colostrinin, a constituent peptide of colostrinin and combination thereof) as the method for inducing a cytokine in a cell, therefore, it would be expected that the treatment of the cell with colostrinin, a constituent peptide of colostrinin or combination thereof produces the desired results (i.e., inhibiting apoptosis or protecting against DNA damage in a cell, or inducing a cytokine in a cell). Since the two methods have the same method steps and would produce the desired results, thus, the method of instant application is obvious variant of the method of the '068 patent. Although the '068 patent is not used for a rejection of the present claims under 35 U.S.C. 102(e) or 103, it does not mean the present claims are not obvious variant of the claims of the '068 patent.

8. Previous rejection of claims 1-6, 8 and 12-15 are rejected under the judicially created doctrine of obviousness-type double patenting as being unpatentable over claims 1-7 of U. S. Patent 7,119,064 is maintained, and new claims 25, 26 and 31-32. Although the conflicting

claims are not identical, they are not patentably distinct from each other because claims 1-6, 8, 12-15, 25, 26 and 31-32 in the instant application disclose a method for inhibiting apoptosis, a method for protecting against DNA damage or a method of modulating an intracellular signaling molecule in a cell, the method comprising contacting the cell with an apoptosis inhibitor or a modulator selected from the group consisting of colostrinin, a constituent peptide of colostrinin (SEQ ID NO:1-8) and combination thereof, and the specification indicates 4-HNE (4-hydroxynonenal) induce apoptosis (Example 7; page 28). This is obvious in view of claims 1-7 of the patent which disclose a method for modulating an intracellular signaling molecule in a cell such as reducing 4-hydroxynonenal (4HNE)-protein adduct formation, inhibiting 4HNE-mediated glutathione depleting, inhibiting 4HNE-induced activation of p53 protein, inhibiting 4HNE-induced activation of c-Jun NH2-terminal kinases, or a method for down regulating 4HNE-mediated oxidative damage associated with lipid peroxidation in a cell, the method comprising contacting the cell with an effective amount of a regulator, wherein the regulator is colostrinin, a constituent peptide of colostrinin (SEQ ID NO:1-8) and combination thereof. Both sets of claims are directed to a method for inhibiting apoptosis or a method for modulating an intracellular signaling molecule in a cell by contacting the cell with an effective amount of colostrinin, a constituent peptide of colostrinin and combination thereof, which is the same method step as encompassed by the two methods. Therefore, claims 1-6, 8, 12-15, 25, 26 and 31-32 in instant application and claims 1-7 of the patent are obvious variations of a method for inhibiting apoptosis or a method for modulating an intracellular signaling molecule in a cell by contacting the cell with an effective amount of colostrinin, a constituent peptide of colostrinin and combination thereof.

Response to Arguments

Applicants indicate that that the present methods of claims 1-6, 8 and 12-15 are patentably distinct from the methods of claims 1-7 of U.S. Patent No. 7,119,064. The Examiner asserted that "the specification indicates 4-HNE (4-hydroxynonenal) induces apoptosis (Example 7, page 28)" (page 7, Office Action mailed October 25, 2006) and thus, the presently claimed method for inhibiting apoptosis and for protecting against DNA damage are "obvious variations" of the methods of claims 1-7 of U.S. Patent No. 7,119,064. Applicants further assert that knowledge that 4-HNE induces apoptosis in no manner substantiates the Examiner's assertion that the presently claimed methods for inhibiting apoptosis and for protecting against DNA damage in a cell are obvious variants of methods "of modulating an intracellular signaling molecule in a cell. Since the method steps and outcomes of pending claims are different from the method steps and outcomes of the '064 patent, the methods cannot be obvious one over the other (pages 10-11 of the response).

Applicants' response has been considered, however, the arguments are not found persuasive because of the following reasons. The specification of instant application teaches 4-HNE (4-hydroxynonenal) induces apoptosis (Example 7, page 28), and colostrinin inhibits apoptosis in a cell. Furthermore, the method for inhibiting apoptosis or protecting against DNA damage in a cell of the pending claims has the same method step (i.e., contacting the cell with an effective amount of colostrinin, a constituent peptide of colostrinin and combination thereof) as the method for modulating an intracellular signaling molecule in a cell of the '064 patent, therefore, it would be expected that the treatment of the cell with colostrinin, a constituent peptide of colostrinin or combination thereof produces the desired results (i.e., inhibiting

apoptosis or protecting against DNA damage in a cell, or modulating an intracellular signaling molecule in a cell). Since the two methods have the same method steps and would produce the desired results, thus, the method of instant application is obvious variant of the method of the '064 patent.

Conclusions

5. No claims are allowed.

Any inquiry concerning this communication or earlier communications from the examiner should be directed to Chih-Min Kam whose telephone number is (571) 272-0948. The examiner can normally be reached on 8.00-4:30, Mon-Fri.

If attempts to reach the examiner by telephone are unsuccessful, the examiner's supervisor, Kathleen Bragdon can be reached at 571-272-0931. The fax phone number for the organization where this application or proceeding is assigned is 571-273-8300.

Information regarding the status of an application may be obtained from the Patent Application Information Retrieval (PAIR) system. Status information for published applications may be obtained from either Private PAIR or Public PAIR. Status information for unpublished applications is available through Private PAIR only. For more information about the PAIR system, see http://pair-direct.uspto.gov. Should you have questions on access to the Private PAIR system, contact the Electronic Business Center (EBC) at 866-217-9197 (toll-free).

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CHIH-MIN KAM
PRIMARY EXAMINER

CMK
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